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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/656,894	WHITT ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2006 and 15 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-112* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,15-18,30-37,42-45,47,49,50,57-62,75,77,79-85 and 89-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 9-14,19-29,38-41,46,48,51-56,63-74,76,78,86-88 and 92-112.

DETAILED ACTION

The previous action mailed 11/1/06 is hereby withdrawn and replaced in its entirety with the following action, This office action is in response to a preliminary amendment filed 10/18/04 and a response to a restriction requirement filed 5/4/06 and 8/15/06. The previously mailed Forms 892 and 1449, however, will not be resent with his office action.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-18, 30-63 and 75-91) and election of 1) methionine 33 substitution, 2) therapeutic polypeptide, 3) GFP, and 4) deletion of residues 440-449 in the reply filed on 5/4/06 and 8/15/06 is acknowledged. The traversal is on the ground(s) that product claims should be rejoined and as such applicants' request rejoinder upon indication of allowance of Group I. This is not found persuasive because the criteria for separating product and process of using have been set forth in the office action mailed 4/5/06. Briefly, the product of Group I can be used in materially different processes of using then those recited in Groups II-VII. As to rejoinder, rejoinder practice has been set forth in the restriction requirement mailed 4/5/06. Briefly, "where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provision of MPEP 821.04. Process claims that depend for or otherwise include all the limitations of the patentable produce will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Furthermore, applicants argue that the species claims should be considered together. Specifically, applicants argue in the response filed 8/15/06 that it is undue burden to search for recombinant non-cytopathic Rhabdovirus with substitution of methionine at position 33 and 51- both positions have been demonstrated to be important for M protein induced cytopathic effects. Applicants arguments filed 5/4/06 and 8/15/06 have been considered but are not persuasive. Applicants claim a Rhabdovirus that has a mutation in amino acid 33 or amino acid 51 and as claimed, these different species of mutations generate structurally distinct viruses that are do not overlap in scope and are not obvious variants that are not used together (see MPEP 806.04 (b)). While the specification teaches that substitution of methionine 33 and 51 are important for M protein induced cytopathic effects, applicants do not claim the mutations used together. Rather, the mutations are separate and the resultant products are distinct structurally.

The requirement is still deemed proper and is therefore made FINAL. Claims 9-14, 19-29, 38-41, 46, 48, 51-56, 63-74, 76, 78, 86-88 and 92-112 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/4/06 and 8/15/06.

Information Disclosure Statement

Information Disclosure Statements filed 5/31/06 and 11/16/04 has been identified and the documents considered. The signed and initialed PTO Form 1449 has been mailed with this action. Documents listed that have not been located have not been considered and have been

crossed out. If applicants want the items listed in the IDS filed 5/31/06 to be considered, new copies of the articles should be sent, accompanied by a new Form 1449.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Specifically, the address of Himangi Jayakar has been altered.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, figures 20 and 21 contain sequences that are not identified by sequence identifier numbers. If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:s. If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:s. If not, a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, CRF and letter stating that the contents of the sequence listing and the CRF are the same and contain no new

matter is required. **The nature of the non-compliance did not preclude the examination on the merits of the instant application, the results of which follow.**

Claim Objections

Claims 5, 34, 45 and 75 are objected to because of the following informalities: Claims 5 and 34 recite "encoding the N-terminal part of said matrix protein encoding a nuclear localization sequence (NLS)". It would be remedial to recite -- encoding the N-terminal nuclear localization sequence (NLS) of said matrix protein -- as it is specifically the N-terminus that encodes the NLS and the claims lack grammatical clarity to indicate that.

Claim 34 recites "said deletion or mutation reside", grammatically, reside in the singular is incorrect. It would be remedial to change "reside" to -- resides--.

Claims 45 and 75 are drawn to "a region encoding a membrane-proximal ectoderm" or "a gene encoding a membrane-proximal ectodomain" of a Rhabdoviral Glycoprotein. For clarity, it is would be remedial to recite -- the membrane proximal ectodomain -- as there is but one ectodomain in the Rhabdoviral Glycoprotein.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 16, 17, 35-37, 42, 47, 49, 50, 58, 59, 61, 62, 77, 79-82, 84, 85 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 35, 47, 77 and 82 are vague and indefinite in that the metes and bounds of the mutations and deletions are unclear. The claims refer to mutations within specific nucleotides that result in substitution of specific amino acids but the claims do not indicate the source sequence to which the amino acids correspond. For example in claims 6, 35, 47 and 82, the mutation results in a substitution in amino acids 33. But applicants do not indicate to what amino acid 33 refers and without a reference sequences it is not clear to what the 33 refers.

Claims 7, 36, 49 and 84 recite the limitation "second polypeptide" in claim 1, 30. There is insufficient antecedent basis for this limitation in the claim as there is no recitation of a first polypeptide.

Claims 16, 61 and 62 provide for the use of the non-recombinant Rhabdovirus as a gene delivery vector or vaccine, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 17 is vague and indefinite in that the metes and bounds of "preferentially cytopathic to neoplastic cells" are unclear. The specification teaches that the Rhabdovirus can be designed to express genes that are cytopathic to tumor cells or neoplastic cells. However, claim 1 does not include cytopathic genes and as such it is unclear if the virus has some structural requirements that result in a virus that is selectively cytopathic in neoplastic cells. As

well, claim 1 does not limit the occurrence of non-cytopathicity so as to make it unclear as to how a virus can be non-cytopathic and cytopathic.

Claim 31 is vague and indefinite in that the metes and bounds of "further comprises a genetically modified glycoprotein (G)". The relationship of the isolated nucleic acid and the protein are unclear as nucleic acids encode the proteins but do not normally comprise them.

Claim 42 is vague and indefinite in that the metes and bounds of "further comprising a Rhabdovirus G stem polypeptide". The relationship of the isolated nucleic acid and the protein are unclear as nucleic acids encode the proteins but do not normally comprise them.

Claim 58 recites the limitation "said genetically modified matrix protein" in claim 57. There is insufficient antecedent basis for this limitation in the claims.

Claim 59 is drawn to a recombinant Rhabdovirus and as such depends from a method of making a Rhabdovirus that appears unrelated to that of claim 59. For example the limitation "said deletion or mutation in said N-terminal part of said matrix protein" in claim 59 has insufficient antecedent basis in claim 73. The structural relationship between the product of claim 59 and the method of claim 73 is unclear. It appears as if the dependency of claim 59 is incorrectly recited.

Claim 75 is vague and indefinite in that the metes and bounds of "a gene encoding a membrane-proximal ectodomain" are unclear. It is unclear how the *gene* can encode a domain or subregion within the protein as genes are responsible for encoding the entire protein.

Claim 79 recites the limitation "said genome of a non-cytopathic Rhabdovirus" in claim 75. The genome of claim 75 is not said to be non-cytopathic and due to the recitation "a", it is

unclear if the non-cytopathic genome is the same genome as that recited in claim 75 or a second genome.

Claim 79 is vague and indefinite in that the metes and bounds of "further comprises a genetically modified matrix protein (M)". The relationship of the isolated nucleic acid and the protein are unclear as nucleic acids encode the proteins but do not normally comprise them.

Claims 80- 82 is vague and indefinite in that the metes and bounds of "said deletion or mutation" and "said mutation" are unclear. Claims 80- 82 is meant to limit the mutations recited in claim 75. However, the mutations of claim 75 are in the G protein of Rhabdovirus and the mutations or deletions of claims 80-82 would be found in the Matrix protein, where the NLS is found. Therefore, it is unclear how said mutations of claim 75 in the G protein can be found in the Matrix protein.

Claim 80 recites "said matrix" in claim 75. There is insufficient antecedent basis for the limitation in the claims.

Claim 89 is vague and indefinite in that the metes and bounds of "further comprising a fusion facilitating polypeptide or an antireceptor". It is unclear how the isolated nucleic acid is to be associated with the fusion facilitating polypeptide or antireceptor. The relationship of the isolated nucleic acid and the protein are unclear as nucleic acids encode the proteins but do not normally comprise them.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 35, 47, 77 and 82 are rejected under are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant Rhabdovirus wherein substitution of an alanine amino acid residue for a methionine at position 33 or 51 or serine for a glycine at amino acid position 226 is in the VSV matrix protein and deletion of residues 440-449 is in the VSV glycoprotein does not reasonably provide enablement for any other embodiments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention**. The instant claims are drawn to a recombinant Rhabdovirus (rRV) comprising mutations in sequences encoding the Matrix protein to generate viruses that are non-cytopathic as well as Rhabdovirus comprising mutations in sequences encoding the membrane proximal ectodomain of the Glycoprotein that has reduced infectivity. In other embodiments, the virus has a mutation in the Matrix and Glycoprotein sequences. The vector is used to deliver therapeutic or immunogenic sequences for treatment purposes.

2) **Scope of the invention**. Claims 6, 35, 47, 77 and 82 are drawn to matrix mutations that are substitutions of methionine 33 with alanine and glycoprotein mutations that are deletion of residues 440-449. The specification teaches that these recited residues correspond to positions in VSV. No other reference sequence is provided such that no correlative site in other Rhabdoviruses is known.

3) **Number of working examples and guidance**. The specification teaches that previous use of rRV as a vector resulted in cytopathic effects and minimal foreign protein expression due to depressed cellular protein synthesis by Matrix protein function. Applicants specifically propose design of vectors that are non-cytopathic due to mutation of amino acids in Matrix protein. The methods require use of the entire VSV genome in which applicants perform site-directed mutagenesis of VSV to isolate cells with no signs of CPE but expressed reporter protein. The following mutations within M were identified; substitution of amino acid 33, 51, 133 and 226 (see e.g. ¶ 222). Applicants also propose deletion of the entire matrix coding sequences and any other mutation that results in reduced of expression of the matrix sequences (page 22, line 1-70. Applicants identify double mutants that have reduced infectivity due to mutations within the glycoprotein (see e.g. example 4). Applicants teach that the G-stem polypeptide refers to a 42 amino acid membrane proximal ectodomain, a transmembrane anchor domain and a cytoplasmic tail domain of mature G protein. Applicants demonstrate that mutations or insertion of 9-10 amino acids within the membrane proximal ectodomain results in suppressed fusion while deletion of amino acids 440-449 abolished fusion activity and deletion of 449-462 diminished infectivity (see e.g. bridging ¶ page 22-23). Applicants identify mutants E452A, G456D, F458A, W461A, G456DW457A, W457AW461A, W457AF458AW461A and G456DW457DW461A as

well as deletion of several domains with the 440-449 and insertion of DAF between 464 and 465 of VSV (see e.g. example 5). .

4) **State of Art**. Rhabdovirus are RNA viruses that comprise six genera including Vesiculoviruses, Lyssavirus and Ephemerovirus obtained from a variety of animal hosts and Novirhabdovirus, cytorhabdovirus and nucleorhabdoviruses are fish, arthropod and plant specific (see Bourhy et al, 2005). At the time of filing (2002), few complete genomic sequences were available and only recently has the available gene-sequence data increased. Current assessment of the taxonomy of the Rhabdoviruses indicates that the major phylogenetic division of the Rhabdoviruses is influenced by mode of transmission and by the host (plant, fish or mammal) and vector (orhtopteran, homopteran or dipteran) species. As well, genetic diversity vary substantially among the genera as demonstrated in figure 3. Vesicular stomatitis virus infection of eukaryotic cells causes inhibition of nuclear transport which is caused by the matrix (M) protein (see e.g. Petersen, 2001, page 8590, col 2, ¶ 1). This thus results in inhibition of host cell gene expression resulting in cytopathic effects in the host cell leading to apoptosis. The G protein is an N-glycosylated class I-transmembrane protein that forms trimers on the viral surface to mediate attachment to cellular receptors, endocytosis and fusion with the vesicular membrane.

5) **Unpredictability of the art**. The MPEP teaches, "However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. Atlas Powder Co. v. E.I. duPont de Nemours &

Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). (see MPEP 2164.08(b).

A review of the art thus demonstrates that the Matrix proteins within the family and even within separate genera are only loosely related. The nucleorhabdoviruses and the Vesiculoviruses share no sequence conservation in the matrix protein (see Luo et al, page 249, col 2, ¶ 2) and even within separate genera; the relationships are not highly conserved. Plant Rhabdoviruses encompass a subgroup of viruses from the Nucleorhabdovirus and the Cytorhabdovirus. Sequence alignment of several of these viruses "have failed to reveal conserved consensus motifs, but short stretches of amino acids display some similarities in composition to the M proteins of other Rhabdoviruses, and the SYNV and RYSV M proteins are more closely related to each other than to other Rhabdovirus proteins" (see Jackson et al, page 642, ¶ 2). Peterson et al provide alignment of 4 highly related Vesiculovirus that demonstrates that inhibition of nuclear transport required a single conserved amino acid which is argued to be due to conserved amino acid correlates to Methionine 51 of VSV (see figure 1). First, this demonstration is limited to only those viruses that are most closely related to VSV. A review of a larger number of Vesiculoviruses show that the relationship amongst the M proteins is not highly conserved (see Marriot, figure 7) with some Vesiculoviruses sharing 22% homology between Matrix protein sequences (see Taylor et al, page 224, col 2, ¶ 3). Secondly, there is absolutely no conservation in the alignment of Peterson et al at amino acids 33 or amino acid 226. Hence, it is highly unpredictable that assignation of sequences by the designation Met 33 or Met 51 will allow one to identify like sequences amongst highly divergent sequences of such a broad and diverse family of viruses. Similarly, the relationship among the G proteins is too low

to allow identification of amino acids 440-449 for any Rhabdovirus. G proteins from different genera share low levels of amino acid sequence identity except for conserved cysteine residues, glycosylation and antigenic domains (see Walker and Kongsuwan, page 1211, col 2, ¶ 1). The plant Rhabdovirus G proteins "have no direct related to G proteins to G proteins of other Rhabdoviruses" (see Jackson et al, page 642, ¶ 2). Walker and Kongsuwan perform a fairly detailed analysis of the structural characteristics of Glycoproteins. Figure 1 is an alignment of 14 species of Rhabdovirus from Vesiculovirus, Lyssavirus, Ephemerovirus and Novirhabdovirus and figure 3 deduced folding models for one from each of these geniuses. The ectodomain is found at the C-terminus of the protein. However, each of the Glycoprotein as well as ectodomains of the proteins have variable length causing confusion as to what actually corresponds to amino acids 440-449. Both the alignment and the models demonstrate that the ability to accurately define the regions that correspond to amino acids 440-449 of the instant specification is highly unpredictable.

6) **Summary**. In view of predictability of the art to which the invention pertains and the lack of guidance in the specification: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Claim Interpretation

Claims 1 and 45 recite that the recombinant non-cytopathic Rhabdovirus comprises **a** nucleic acid of a Rhabdoviral genome. There are two possible interpretations of the phrase "a nucleic acid of a Rhabdoviral genome. First, a Rhabdoviral nucleic acid is any as long as it is at least a dinucleotide and based upon this interpretation, the claims are drawn to a recombinant non-cytopathic virus comprising at least a dinucleotides of sequences found in a Rhabdovirus. Secondly, the nucleic acid encodes the entire Rhabdoviral genome and based upon this interpretation the entire Rhabdovirus genome is encompassed by the claims. Secondly, claims 31, 42, 79 and 81 are drawn to isolated nucleic acid comprising either glycoprotein or Matrix protein. For purposes of examination, these claims are interpreted to encompass nucleic acid encoding glycoprotein or Matrix protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7, 8, 15-18, 30-34, 36, 37, 43- 45, 47, 49, 50, 57, 58, 60-62, 75, 77, 79-81, 83-85 and 89-91 are rejected under 35 U.S.C. 102(e) as being anticipated by Bell et al (2004/0170607; see entire documents).

This art rejection is based upon an interpretation of the claims that **a** nucleic acid encodes the entire Rhabdoviral genome.

Bell et al teach recombinant Rhabdovirus that are mutants of VSV with impaired shut-down of host protein synthesis (see e.g. ¶ 103) such as mutant 4 (M4) comprising a mutation in the NLS signal as recited in claims 1, 4, 5, 18, 30, 33, 34, 43, 80, 81 and 90. As well, the VSV viruses comprise sequences coding for G stem polypeptide as recited in claims 15 (see e.g. figure 21-2) and these G proteins are modified (see e.g. figure 20). For example, the mutant HR (see figure 21-2) comprises mutations in the matrix domain as well as deletions in the region within the membrane proximal ectodomain that corresponds to 440-449 of the instant specification, as recited in claims 45, 47, 75 and 77. Hence, the Rhabdovirus comprises mutations in the M protein in addition to modifications within the G protein as recited in claims 2, 31, 57, 58 and 79. The G protein is modified (see e.g. ¶ 112) such that the RV expresses for example therapeutic proteins (see e.g. ¶ 113-114) or to encode antireceptors (see e.g. ¶ 112) as recited in claims 7, 8, 36, 37, 49, 50, 84, 85 and 89. The coding sequences is inherently under control of a regulatory element as recited in claims 3, 32, 60 and 83. The Rhabdovirus are vectors designed to act as gene delivery vectors and to deliver antigens as recited in claim 16, 44, 61, 62 and 91 for delivery to cells (see e.g. ¶ 112). Bell et al isolated viruses that selectively kill tumor cells but is non-cytopathic in normal cells (see e.g. example 2) as recited in claim 17.

Claims 1-8, 15-18, 30-34, 36, 37, 43- 45, 47, 49, 50, 57, 58, 60-62, 75, 77, 79-81, 83-85 and 89-91 are rejected under 35 U.S.C. 102(e) as being anticipated by Bell et al (2004/0170607; see entire documents).

This art rejection is based upon an interpretation of the claims that **a** nucleic acid a Rhabdoviral nucleic acid is any as long as it is at least a dinucelotide and based upon this interpretation, the claims are drawn to a recombinant non-cytopathic virus comprising at least a dinucleotides of sequences found in a Rhabdovirus.

In addition to the reasons above, the Rhabdovirus of Bell et al also anticipates claims 6. In this case, the Rhabdovirus of Bell et al need not comprise the part of the genome that comprises mutation in the matrix genes.

Claims 1-3, 7, 8, 15, 16, 18, 30, 32, 36, 37, 43-45, 47, 49, 50, 60-62, 75, 77, 83-85 and 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Conzelmann (US 6,033,886; see entire document).

This art rejection is based upon an interpretation of the claims that **a** nucleic acid encodes the entire Rhabdoviral genome.

Conzelmann teaches a recombinant non-cytopathic Rhabdovirus such as VSV (see e.g. col 5, line 39 and col 3-4 bridging ¶) comprising a genome comprising a mutation in the M protein (M-) (see e.g. col 6, line 5-6) or a mutation or deletion in the sequence encoding a G protein (G-) (see e.g. col 6, line 29-30) as recited in claims 1, 2, 18, 30, 43, 45, 75 and 90. As the only mutation in the M- Rhabdovirus is in the matrix sequence, the Rhabdovirus inherently comprises a G stem polypeptide as recited in claim 15. In the G- Rhabdovirus, the mutation/ deletion in the G sequence can be the entire sequence and as such encompass a deletion in the 440-449 region (see e.g. col 6, line 36) as recited in claims 47 and 77. The Rhabdovirus inherently comprises a regulatory region for expression of its proteins as recited in claim 3, 32,

60 and 83. The virus comprises heterologous nucleic acids encoding sequences that can be considered therapeutic in that they are used to generate therapies against virulent viruses (see e.g. col 3,line 30-33) as recited in claims 7, 8, 16, 36, 37, 49, 50, 61, 62, 84 and 85 and are additionally inherently associated with regulatory elements for their expression as recited in claims 3, 32, 60 and 83. The heterologous nucleic acids can be epitopes, which often function as anti-receptors as recited in claim 89. Vectors encoding the genomes are taught in col 11, line 10-12 as recited in claims 44 and 91.

Claims 1-8, 15, 16, 18, 30, 32, 36, 37, 42-45, 47, 49, 50, 60-62, 75, 77, 83-85 and 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Conzelmann (US 6,033,886; see entire document).

This art rejection is based upon an interpretation of the claims that **a** nucleic acid a Rhabdoviral nucleic acid is any as long as it is at least a dinucelotide and based upon this interpretation, the claims are drawn to a recombinant non-cytopathic virus comprising at least a dinucleotides of sequences found in a Rhabdovirus.

In addition to the reasons above, the Rhabdovirus of Conzelmann also anticipates claims 4-6. In this case, the Rhabdovirus of Conzelmann need not comprise the part of the genome that comprises mutation in the matrix and/or glycoprotein genes.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45, 75 and 90 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 7, 8 and 28 of copending Application No. 10/274,359.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of the instant invention are generic to all that is recited in claims 1, 3, 7, 8 and 28 of copending Application No. 10/274,359. That is, the cited claims of copending Application No. 10/274,359 anticipate and fall entirely within the scope of the rejected claims of the instant application. Specifically, claim 8 of copending Application No. 10/274,359 claims a recombinant Rhabdovirus comprising potential

deletions of G peptide sequences and DNA sequences encoding the Rhabdovirus with the exception of G peptide.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding the copending Application No. 10/274,359, then two different assignees would hold a patent to the claimed invention of copending Application No. 10/274,359, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45, 47, 49, 61, 75, 77, 83, 84 and 89-91 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/327,673.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of the instant invention are generic to all that is recited in claims 1-20 of copending Application No. 10/327,673. That is, the cited claims of copending Application No. 10/327,673 anticipate and fall entirely within the scope of the rejected claims of the instant application. Specifically, copending Application No. 10/327,673 claims a recombinant Rhabdovirus comprising a deletion of N-terminal sequences of a VSV G peptide sequence and DNA sequences encoding the Rhabdovirus.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding the copending Application No. 10/327,673, then two different assignees would hold a patent to the claimed invention of copending Application No. 10/327,673, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633